REMARKS

The specification has been amended to insert a dessignation of the circles and squares with respect to the brief description of Figures 6 and 7. Support for this insertion can be found in paragraph [0039] on page 8.

Claim 1 has been amended to delete the word "essentially" with respect to the "stable product" of steps (a)(i) and (a)(iii) and to clarify that the "a" in these same steps refers to step (a).

It is submitted that these amendments do not constitute new matter and their entry is requested.

The Examiner rejected claims 1-10 under 35 U.S.C. § 112, first paragraph for lack of enablement. It is submitted that the Examiner is in error in this rejection.

Specifically, Applicants note that the Examiner has not set forth an analysis of the *Wands* factors as required by the Patent Office's guidelines for enablement rejections. Thus, the Examiner has not presented a *prima facie* case of lack of enablement.

In addition, the "examiner has the initial burden to establish a reasonable basis to question the enablement provided for the **claimed** invention." MPEP2164.04, *citing In re Wright*, 999 F.2d 1557, 1562, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir.1993) (emphasis added). Furthermore, it is incumbent upon the Patent Office to

> "explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure."

M.P.E.P. § 2164.04, *citing In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971).

The Examiner merely contends that the specification is not enabled for other groupings of reporter genes. Such a contention, without scientific reasons or evidence, is not sufficient to sustain an enablement rejection. *In re Marzocchi*. As provided in the M.P.E.P., if doubt arises about enablement because information is missing about one or more essential parts or relationships

between parts which one skilled in the art could not develop without undue experimentation, the examiner "should specifically identify what information is missing and why one skilled in the art could not supply the information without undue experimentation." M.P.E.P., 2164.04. Furthermore, while references may not be required for the Examiner to meet his or her burden, "specific technical reasons are **always** required. *Id.* (emphasis added). To determine enablement, the specification is considered in light of the knowledge in the art at the time of the invention. When considering the adequacy of enablement for a generic claim, the M.P.E.P. states that proof of enablement is required for other members of the genus "...only where **adequate reasons** are advanced by the Examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation." M.P.E.P. at 2164.02.

Furthermore, other genes were well known in the art, including those disclosed by Grentzmann et al. (US 6,143,502) cited by the Examiner. Other known genes have been described in Tsien ("Bioluminescence," *Annu Rev Biochem* **67**:509-544, 1998) and Wilson and Hastings ("The green fluorescen protein," *Annu Rev Cell Biol* **14**:197-230, 1998).

In view of the above remarks, it is submitted that the claims are fully enabled by the specification. Withdrawal of this rejection is requested.

The Examiner rejected claims 1-10 under 35 U.S.C. § 112, second paragraph for being indefinite. Claim 1 has been amended to clarify the language of the claim.

In view of the amendments to the claims and the above remarks, it is submitted that the claims are definite. Withdrawal of this rejection is requested.

The Examiner rejected claims 1-4 and 6-7 under 35 U.S.C. § 102 (e) as being anticipated by Szalay et al. (US 5,976,796). It is submitted that the Examiner is in error in this rejection.

Specifically, Szalay et al. only discloses the measurement of gene expression in live cells. It does not describe or suggest the measurement of gene expression in other cells. In addition, Szalay et al. does not disclose or suggest the assessment required by step (c) of claim 1. Furthermore, Szalay et al. does not disclose or suggest that by using (at least) two markers, each correlating with

a different member of the group -- the cells that have lived, the cells that are alive and the cells that have died – one can assess the growth rate and death rate of the microorganism. It is a clear advantage, which results from the present invention, to be able to differentiate between actual growth rate and apparent growth rate (in case the overall live cell count is rising) on the one hand and actual death rate and apparent death rate (in case the overall live cell count is decreasing) on the other hand in an environment of interest. Thus, it can separately be determined how the environment affects the growth rate as such and the death rate as such of the microorganism.

In view of the amendments to the claims and the above remarks, it is submitted that the claimed subject matter is not anticipated by Szalay et al. Withdrawal of this rejection is requested.

The Examiner rejected claims 1-10 under 35 U.S.C. § 103 (a) as being obvious over Fratamico et al. (*J Food Protection* **60**:1167-1173, 1997) in view of Brovko et al. (*Proceedings of SPEI - The International Society of Optical Engineering* **3921**:147-156, 2000) and Wang et al. (Pro. 9th Int Sym on Bioluminescence and chemiluminescence, pages 419-422, 1996). It is submitted that the Examiner is in error in this rejection.

Specifically, Applicants note that Brovko et al. was published in April 2000, subsequent to the 7 June 1999 priority date of Finnish patent application 991296. Since the certified copy of this priority application has been received, as acknowledged by the Examiner in the present Office Action, and the Finnish application is in English, Brovko et al. is not a proper reference to the present application. Thus, Brovko et al. is not available to be combined with Fratamico et al. and Wang et al.

Fratamico et al. merely discloses the use of GFP to measure livability. Wang et al. merely discloses the functionality of a luciferase-modified GFP protein. None of these references, however, discloses or suggests that by using (at least) two markers, each correlating with a different member of the group -- the cells that have lived, the cells that are alive and the cells that have died – one can assess the growth rate and death rate of the microorganism. It is a clear advantage, which results from the present invention, to be able to differentiate between actual growth rate and apparent

growth rate (in case the overall live cell count is rising) on the one hand and actual death rate and apparent death rate (in case the overall live cell count is decreasing) on the other hand in an environment of interest. Thus, it can separately be determined how the environment affects the growth rate as such and the death rate as such of the microorganism.

In view of the amendments to the claims and the above remarks, it is submitted that the claimed subject matter is not obvious over Fratamico et al. in view of Brovko et al. and Wang et al. Withdrawal of this rejection is requested.

In view of the above amendments and remarks, in conjunction with the remarks made in the previous amendment, it is believed that the claims satisfy the requirements of the patent statutes and are patentable over the prior art. Reconsideration of the instant application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

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